Please add the following new claims:

48. The method according to claim 18 wherein the fibronectin is RetroNectin™ .

49. The method according to claim 23 wherein the fibronectin is RetroNectin™ .

50. The method according to claim 37 wherein the fibronectin is RetroNectin™ .

51. The method according to claim 37, wherein said human hematopoietic cells are $CD34^{+}Thy\text{-}1^{-}$ cells.

Please cancel claims 28, 36 and 45.

REMARKS

Claims 18 - 20, 23 - 27, and 31 - 35, 37 - 44 and 46 - 50 are pending in the instant application. Claims 28, 36 and 45 have been canceled. Claims 18, 23 and 37 have been amended and claims 48 – 51 are added by the present amendment.

In the Office Action dated October 27th, the Examiner objected to claims 28 and 45 as being dependent upon a rejected base claim, but allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims. Claim 28 was dependent on independent claim 23, and claim 45 was dependent on independent claim 37. Applicants have amended independent claims 23 and 45 to incorporate the subject matter of claims 28 and 45. Applicants believe these claims, and the claims dependent thereon, are in form for allowance. Additionally independent claim 18 has been amended to include the subject matter of claims 28 and 45. It is respectfully suggested that this claim should also be allowable.

Applicants have added new claims 48 – 50. These claims recite that the fibronectin is RetroNectin™ . Support is found in original claim 28 and in the specification. In addition, Applicants have added new claim 51. This claim recites a specific subpopulation of hematopoietic cells as being $CD34^{+}Thy\text{-}1^{-}$. Support is found throughout the specification, and more particularly on page 15.

In paper number 6, claims 18 – 20, 23 – 27, 31, 37 – 44 and 46 – 47 were rejected by the Examiner under 35 U.S.C. 103 (a) as being unpatentable over Murray et al. (USP 5,665,557), Nakahata (USP 5,861,315), Hoffman et al. (USP 5,744,361), Fei et al. (USP 5,635,387), or Davis et al. (USP 5,599,703), in view of Ku et al., Kobayashi et al., Ramsfjell et al. (IDS Reference AK), Ohmizono et al., Szilvassy et al., Escary et al., or Bodine et al., and further in view of Tushinski et al. (IDS reference AN), Fletcher et al., Bello-Fernandez et al., or Hatzfeld et al. There are no other rejections pending in the application, and the previous rejection of claims 18 – 30, in paper number 3, under 35 U.S.C. 112, first paragraph has not been maintained.

Applicants respectfully traverse the rejection under 35 U.S.C. 103. However, in view of the Examiner's statement of allowable subject matter, Applicants have decided to expedite allowance of this application by incorporating fibronectin as a component of the culture in the culturing step and to prosecute the rejected claims, directed to the cytokines, in further continuation applications. Applicants emphasize that the decision to not prosecute the rejected claims in the present application is not an acquiescence that the references cited by the Examiner render the claims obvious under 35 U.S.C. 103.

Applicants kindly solicit allowance of claims 18 – 20, 23 – 27, 31 – 35, 37 – 44 and 46 – 51. A clean copy of the pending claims is attached as Appendix A.

Respectfully submitted,

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APPENDIX A - Clean Copy of Proposed Pending Claims

18. A method for genetically modifying human hematopoietic stem cells, comprising:

a) contacting a vector comprising a polynucleotide sequence encoding a heterologous gene with a population of hematopoietic stem cells cultured with fibronectin and in the presence of an effective amount of a mpl ligand and a flt3 ligand each ligand provided in a concentration range of about 0.1 ng/mL to about 500 ng/mL, wherein said vector is selected from the group consisting of retroviral vectors, adenoviral vectors, and adeno-associated viral vectors; and

b) obtaining modified human hematopoietic stem cells.

19. The method according to claim 18, further comprising culturing the hematopoietic stem cells in the presence of a c-kit ligand in a concentration range of about 5 ng/mL to about 200 ng/mL.

20. The method according to claim 19, further comprising culturing the hematopoietic stem cells in the presence of a interleukin 3 (IL3) in a concentration range of about 5 ng/mL to about 200 ng/mL.

23. A method for genetically modifying human hematopoietic stem cells, comprising:

a) contacting a vector comprising a polynucleotide sequence encoding a heterologous gene with a population of hematopoietic stem cells cultured with fibronectin and in the presence of an effective amount of a thrombopoietin ligand (TPO), a flt3 ligand (FL), and interleukin 6 (IL6) wherein the TPO, FL and IL6 are each provided in a concentration range of about 0.1 ng/mL to about 500 ng/mL, and wherein said vector is selected from the group consisting of retroviral vectors, adenoviral vectors, and adeno-associated viral vectors; and

b) obtaining modified human hematopoietic stem cells.

24. The method of claim 23, further comprising culturing the stem cells in the presence of an effective amount of leukemia inhibitory factor (LIF) wherein said effective amount is in the range of 5 ng/mL to about 200 ng/mL.

25. The method of claim 23, further comprising culturing the stem cells in the presence of an effective amount of interleukin 3 (IL3) wherein the effective amount is in the range of about 10 ng/mL to about 100 ng/mL.

26. The method of claim 23, further comprising culturing the stem cells in the presence of a c-kit ligand wherein said effective amount is in the range of 5 ng/mL to about 200 ng/mL.

27. The method of claim 25, further comprising culturing the stem cells in the presence of a c-kit ligand wherein said effective amount is in the range of 5 ng/mL to about 200 ng/mL.

31. The method according to claim 23, wherein the effective amount of TPO and FL individually is in the range of about 5 ng/mL to about 200 ng/mL and the effective amount of IL6 is in the range of about 10 ng/mL to about 100 ng/mL.

32. The method according to claim 23, wherein the vector is a retroviral vector.

33. The method according to claim 23, wherein the heterologous gene is a marker gene.

34. The method according to claim 23, further comprising expanding the modified human hematopoietic cells.

35. The method according to claim 23, wherein the human hematopoietic cell is a $CD34^+$ $Thy\text{-}1^+$ Lin^- cell.

37. A method of transducing mammalian $CD34^+$ hematopoietic cells including a subpopulation of hematopoietic stem cells comprising,

(a) obtaining a source of hematopoietic cells including the subpopulation of hematopoietic stem cells;

(b) culturing said cells with the cytokines TPO, FL and IL-6, individually provided in the range of about 0.1 ng/mL to about 500 ng/mL;

(c) infecting the cultured cells with a retroviral vector including a polynucleotide sequence encoding a heterologous gene; and

(d) obtaining transduced cells wherein said gene is expressed.

38. The method according to claim 37, wherein the TPO, FL and IL-6 are individually provided in the range of about 5 ng/mL to about 200 ng/mL.

39. The method according to claim 37, further comprising culturing the cells in the presence of an effective amount of leukemia inhibitory factor (LIF) wherein said effective amount is in the range of 5 ng/mL to about 200 ng/mL.

40. The method according to claim 37, further comprising culturing the cells in the presence of an effective amount of IL-3 wherein said effective amount is in the range of 10 ng/mL to about 100 ng/mL.

41. The method according to claim 39, further comprising culturing the cells in the presence of an effective amount of IL-3 wherein said effective amount is in the range of 10 ng/mL to about 100 ng/mL.

42. The method according to claim 37, wherein the effective amount of IL-6 is in the range of about 10 ng/mL to about 100 ng/mL

43. The method according to claim 37, wherein the TPO is provided as a mimetic.

44. The method according to claim 37, wherein said human hematopoietic cells are $CD34^{+}Thy\text{-}1^{+}$ Lin^{-} cells.

46. The method according to claim 37, wherein the heterologous gene is a marker gene.

47. The method according to claim 37, wherein the heterologous gene is a therapeutic gene.

48. The method according to claim 18 wherein the fibronectin is RetroNectin™.

49. The method according to claim 23 wherein the fibronectin is RetroNectin™.

50. The method according to claim 37 wherein the fibronectin is RetroNectin™.

51. The method according to claim 37, wherein said human hematopoietic cells are $CD34^{+}Thy\text{-}1^{-}$ cells.